

**REMARKS/ARGUMENTS**

Claims 1-19 were pending in the instant application. Claims 5, 14 and 18 have been cancelled without prejudice. Claims 1, 3, 6 and 10 have been amended and claims 20-22 have been added to more particularly point out and distinctly claim that which Applicants consider to be their invention.

Upon entry of the above-made amendments claims 1-5, 6-13, 15-17 and 19-22 will be pending in the current application. The amended claims and newly added claims are fully supported in the specification as originally filed. Therefore, the amendments to the claims do not add new matter. Applicants respectfully request that the amendments be entered.

The following remarks, in conjunction with the above amendments, are believed to be fully responsive to the Office Action.

**THE REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH**

**SHOULD BE WITHDRAWN**

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. In particular, the Examiner contends that it is unclear whether the feature introduced by a narrow language is merely exemplary or a required element. In response,

Applicants submit that claim 10 has been amended to remove the objectionable language and the preferred embodiments are now claimed in claims 20 and 21.

Further, claims 14 and 18 are rejected under 35 U.S.C. 101 for failing to set forth any steps involved in the process. In response, Applicants have cancelled claims 14 and 18.

Therefore, Applicants respectfully request that the rejections of the 35 U.S.C. 112, second paragraph, of claim 10 and rejections under 35 U.S.C. 101 of claims 14 and 18 be withdrawn.

**THE REJECTIONS UNDER 35 U.S.C. § 102  
SHOULD BE WITHDRAWN**

Claims 1-6 and 15-18 are rejected under 35 U.S.C. § 102(b) as being anticipated by US patent no. 6,096,720 ("Love"). In response, Applicants submit that each of the rejections should be withdrawn for the reasons stated below.

As noted above, claim 1 has been amended to include feature (a\*) the corresponding (PEG)-modified compound of (a) 1-acyl-2-acyl-glycero-3-phosphoethanolamine-PEG (a\*) (emphasis added).

Love relates to compositions comprising oligonucleotides targeted to mRNA encoding human raf and capable of inhibiting raf expression. These oligonucleotides are

entrapped in liposomes. As Love explains at column 7, lines 37-40, in one preferred embodiment, the liposomes comprises at least one underivatized vesicle-forming lipid and at least one vesicle-forming lipid derivatized with hydrophilic polymer. In this embodiment, both the derivatized and the underivatized vesicle-forming lipid can be a 1-acyl-2-acyl-glycerol-3-phosphoethanolamine, for example dimyristoyl phosphatidyl ethanolamine. The polymer can be derivatized with PEG (column 7, lines 41-42). Therefore, this embodiment of Love is equivalent to a combination of features (a) and (a\*) of amended claim 1 of the present application and does not contain any ingredient according to feature (b) of amended claim 1 of the present application

In an alternative preferred embodiment of Love, the liposomes comprise (i) a glycolipid together with (ii) a vesicle-forming phospholipid or sphingolipid or a mixture thereof and optionally (iii) a sterol and/or an acylglycerol (column 8, lines 37-41).

As with the previous preferred embodiment, the vesicle-forming phospholipid (i) can be a 1-acyl-2-acyl-glycerol-3-phosphoethanolamine. The acylglycerol lipid (iii) can be 1,2-dipalmitoyl-sn-3-succinyl glycerol (column 8, lines 61-62), which is equivalent to feature (b) of amended claim 1 of the present invention. Thus, the alternative preferred embodiment of Love comprises (i) a 1-acyl-2-acyl-glycerol-3-phosphoethanolamine (feature (a) of amended claim 1), (ii) a vesicle-forming phospholipid or sphingolipid (not present in the liposomes of the present invention) and (iii) a 1-acyl-2-acylsuccinylglycerol or 1-acyl-3-acylsuccinylglycerol (feature (b) of amended claim 1).

Therefore, the first preferred embodiment of Love comprises features (a) and (a\*) of amended claim 1, while the second preferred embodiment comprises features (a) and (b) of amended claim 1 and additionally a vesicle-forming phospholipid or sphingolipid which is not present in the liposomes of the present invention.

These embodiments are alternatives and thus there is no teaching in Love of a liposome with all of the features of amended claim 1. Furthermore, there is no reason why a person of skill in the art would be motivated to combine these two alternative embodiments.

The important feature of the liposomes of Love is that they must be sterically stabilized as they are intended for the delivery of an oligonucleotide to a tumor. In contrast, the liposomes of the present invention are intended for the preparation of pH sensitive paramagnetic MR contrast agents for *in vivo* applications. Important features of the liposomes of the present invention are that they must be pH sensitive and remain pH sensitive in human blood; they must be relatively impermeable to water; and the blood circulation time should also be as long as possible. As explained on page 5, lines 7-14, blood circulation time can be increased by including a proportion of the PEGylated component (a\*) in the liposome, although the amount of (a\*) should be optimised to ensure that both the blood residence time and the pH sensitivity are suitable.

Since Love were not concerned with pH sensitivity or blood circulation time of the liposomes, there would have been no reason for a person of skill in the art to combine

selected features of the different preferred embodiments of Love to arrive at the liposome system of the currently amended claim 1.

Thus, Applicants respectively submit that amended claim 1 is neither anticipated by nor obvious in the light of Love. Claims 2-6 are dependent on claim 1 and therefore Applicant believes that these claims are also new and non-obvious over Love. Similarly, Applicants submits that claims 15-18, which relate to compositions and methods of treatment using the liposomes of claim 1, are also new and non-obvious over Love. Applicants respectfully request that the 35 U.S.C. 102 rejections over Love be withdrawn.

**THE REJECTIONS UNDER 35 U.S.C. § 103  
SHOULD BE WITHDRAWN**

Claims 1 and 7-19 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Love in view of US 5,159,445 ("Klaveness"). In response, Applicants submit that each of the rejections should be withdrawn for the reasons stated below.

The Examiner argues that Love teaches the liposomes of claim 1 but does not teach imaging or contrast agents. However, Klaveness is said to teach that contrast agents encapsulated in liposomes are known in the art and are useful in light imaging methods.

As stated above, claim 1 has now been amended and Applicant submits that Love does not teach all of the features of claim 1. In particular, Love relates to two distinct

embodiments, one of which has features (a) and (a\*) of amended claim 1 and the other of which has features (a) and (b) of amended claim 1, together with a third component which is not a feature of the liposomes of the present invention.

Applicant further submits that Klaveness does not contain all of the necessary features to arrive at the claims 7-19 of the present application – i.e. it does not teach a liposome having features (a), (a\*) and (b) of amended claim 1.

In addition, although it is known from Klaveness that contrast agents can be encapsulated in liposomes, there would have been no motivation to use the liposomes of Love for encapsulation. Love is not concerned with contrast agents and therefore the liposomes it teaches do not have to be pH sensitive or relatively impermeable to water. These are essential features of the liposomes of the present invention. Applicants therefore submit that one of skill in the art would not have been motivated to combine the documents.

In view of the foregoing, it is therefore respectfully submitted that 35 U.S.C. 103 rejections of claims 1 and 7-19 over Love in view of Klaveness be withdrawn.

### **CONCLUSION**

In view of the amendments and remarks herein, applicants believe that each ground for rejection or objection made in the instant application has been successfully overcome or obviated, and that all the pending claims are in condition for allowance. Withdrawal of the

Appl. No. 10/753,929  
Amdt. Dated Sep. 10, 2007  
Reply to Office action of June 22, 2007

Examiner's rejections and objections, and allowance of the current application are respectfully requested.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

/Li Cai/  
Li Cai  
Reg. No. 45,629

GE Healthcare, Inc.  
101 Carnegie Center  
Princeton, NJ 08540  
Phone (609) 514-6418

E:\IP\Response to Office Action\PN\PN0301 (09-10-07).doc